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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Stanton et al.	) Group Art Unit 1634
Appl. No.	:	09/665,976	)
Filed	:	September 20, 2000	)
For	:	SECRETED FACTORS	)
Examiner	:	Jehanne E. Souaya	)

AMENDMENT AND RESPONSE TO OFFICE ACTION

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

In response to the Office Action mailed on April 18, 2002 (Paper No. 12), please consider the following remarks and amendments.

In the Claims:

Please amend claims 1, 5 and 6 to read as follows:

1. Claim 1. (Twice Amended) An isolated nucleic acid molecule comprising a poly- or oligonucleotide selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide having at least 90% sequence identity with SEQ ID NO: 1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardial disease model;

(b) a polynucleotide encoding a polypeptide having at least 90% sequence identity with amino acids 25 to 236 of SEQ ID NO: 1;

(c) a polynucleotide encoding a polypeptide having at least 90% sequence identity with amino acids 25 to 214 of SEQ ID NO: 1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model;

(d) a polynucleotide encoding amino acids 25 to 236 of SEQ ID NO: 1, or a transmembrane domain deleted or inactivated variant thereof, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardial disease model;

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(e) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25 to 214 of SEQ ID NO: 1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardial disease model;

(f) a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25 to 236 of SEQ ID NO: 1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardial disease model; and

(g) the complement of a polynucleotide of (a) – (f).

Claim 5. (Amended) A vector comprising and expressing a poly- or oligonucleotide of claim 1.

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Claim 6. (Amended) A recombinant host cell transformed with a nucleic acid comprising a poly- or oligonucleotide of claim 1.

Please add the following claims:

Claim 30. (New) An isolated polynucleotide encoding a polypeptide comprising a native mammalian homologue having at least 90% amino acid sequence identity to SEQ ID NO: 1, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model.

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Claim 31. (New) An isolated polynucleotide comprising SEQ ID NO: 2 or the region of SEQ ID NO: 2 that codes for the polypeptide of SEQ ID NO 1.

Claim 32. (New) An isolated polynucleotide that hybridizes to the region of SEQ ID NO: 2 that codes for the polypeptide of SEQ ID NO 1 or to the complement of the region of SEQ ID NO: 2 that codes for the polypeptide of SEQ ID NO 1 under stringent hybridization conditions of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, 50 μg/ml salmon sperm DNA, 0.1% SDS, and 10% dextran sulfate at 42°C, and wash conditions of 0.2x SSC and 50% formamide at 55°C, followed by 0.1x SSC with EDTA at 55°C, wherein the complement of said polynucleotide detects, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model.

Claim 33. (New) The polynucleotide of claim 32, wherein said polynucleotide encodes a polypeptide having at least 90% sequence identity with the polypeptide of SEQ ID NO: 1.

REMARKS

Claims 1-7 were pending in this application. Claims 1 and 6 were amended, and new claims 30-33 have been added to further clarify the invention. The amendments to claims 1 and 6 are supported in the specification, for example, on page 11, line 32 to page 12, line 3; page 49, lines 15-19; page 16, lines 12-20; page 16, lines 21-28; page 20, line 25, through page 23, line 30; pages 56-66, Example 1; page 71, Example 8; and page 74, lines 21-25.

Support for new claim 30 is found in the specification, for example, on page 11, line 32 to page 12, line 4. Support for new claim 31 is found in the specification, for example, on page 7, lines 23-27, and in Figure 2. Support for new claim 32 is found in the specification, for example, on page 13, lines 5-11. Support for new claim 33 is found in the specification, for example, on page 11, line 32 to page 12, line 4. No new matter is added by any of the foregoing amendments.

Objections

Claim 6 was objected to "because of the following informalities: the recitation of the phrase 'nucleic acid' lacks the article 'a'." The amendment to claim 6 as suggested by the Examiner is believed to overcome the present objection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-7 were rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

(1) Specifically, claim 1, in sections a, b, e and f was rejected as "indefinite over the phrase 'at least about' because the metes and bounds of the invention are not clear." The current amendment to claim 1 which no longer recites "at least about" is believed to overcome the present rejection.

(2) Claim 1, in section c, was rejected as "indefinite in the recitation of 'or inactivated variant' as it is unclear if the 'activated variant' refers to a polypeptide where the transmembrane domain is inactivated or whether any portion of the polypeptide could be inactivated." The current amendment to claim 1 which no longer recites "or inactivated variant" is believed to overcome the present rejection.

(3) Claim 1, in section d, was rejected as "indefinite in the recitation of 'stringent conditions' as this language encompasses different reaction conditions such that the degree of complementarity needed to achieve hybridization between the nucleic acid sequence claimed and SEQ ID NO 2 is unclear." The current amendment to claim 1 which no longer recites "stringent conditions" is believed to overcome the present rejection. Applicants further point out that although new claim 32 cites "stringent hybridization conditions," the specific conditions are clearly specified and that the metes and bounds of the claim are clear.

(4) Claim 1, in section d, was rejected as "indefinite in the recitation of 'coding region of SEQ ID NO: 2' because it cannot be determined if this phrase refers to the region that codes for the polypeptide of SEQ ID NO 1 or if it refers to the whole length of SEQ ID NO 2, which in figure 2 is shown to code for a number of amino acids on either side of the polypeptide of SEQ ID NO 1." The current amendment to claim 1 which no longer recites "coding region of SEQ ID NO: 2" is believed to overcome the present rejection.

As there is no vagueness or indefiniteness in the language of claim 1, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(5) Claim 5 was rejected as "indefinite in the recitation of the term 'capable' as it is unclear if the claimed product actually exhibits the function of expressing a poly or

oligonucleotide of claim 1 or whether the claim encompasses that it 'could' exhibit this function but does not." The current amendment to claim 5 which no longer recites "capable" is believed to overcome the present rejection.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-2 and 5-7 were rejected under 35 U.S.C. 112, first paragraph, because "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims." The Examiner specifically pointed out that the specification does not provide enablement for a nucleic acid molecule comprising: a polynucleotide encoding a polypeptide having at least about 80% sequence identity with amino acids 25-236 of SEQ ID NO 1, a polynucleotide encoding a polypeptide having at least about 80% sequence identity with amino acids 25 to 214 of SEQ ID NO 1, a transmembrane domain deleted or inactivated variant of a polynucleotide encoding amino acids 25 to 236 of SEQ ID NO 1, a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO 2 and encoding a polypeptide having at least one biological activity of the polypeptide encoded by SEQ ID NO 2, a polynucleotide encoding at least about 50 contiguous amino acids 25-214 of SEQ ID NO 1 wherein the polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by SEQ ID NO 2, a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25-236 of SEQ ID NO 1 wherein the polynucleotide encodes a polypeptide having at least one biological activity of SEQ ID NO 1, complements thereof, a polynucleotide encoding a polypeptide comprising amino acids 25 to 214 of SEQ ID NO: 1, or vectors and host cells comprising such. The Examiner, however, acknowledged that the specification provides enablement for "an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide comprising SEQ ID NO 1, an isolated nucleic acid molecule encoding amino acids 25 to 236 of SEQ ID NO 1, an isolated nucleic acid molecule comprising the sequence of SEQ ID NO 2, the complement thereof, and a vector or host cell comprising such."

Without acquiescing in the Examiner's position, and merely to facilitate the prosecution of the present application, Applicants have amended claim 1. Claim 1 has been amended to recite "polynucleotides that encode a polypeptide having at least 90% sequence identity with SEQ ID NO: 1" or to specific regions thereof, which is fully supported by the specification as

originally filed. One of ordinary skill in the art would reasonably conclude that a polynucleotide encoding a polypeptide with 90% identity to SEQ ID NO; 1 shares a common utility with a polynucleotide encoding SEQ ID NO: 1 itself. This conclusion is based on the fact that polynucleotides encoding highly similar polypeptides share significant sequence identity and are more likely than not useful for the same purpose. Applicants have also amended claim 1 to recite a polynucleotide whose complement "detects, by microanalysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model," which is fully supported by the specification at pages 62-65. One of ordinary skill in the art would reasonably conclude than any polynucleotide possessing this limitation would have a specific and substantial utility, for example, as a diagnostic marker or probe for myocardial infarction. Therefore, any polynucleotide species that falls within the scope of claim 1 possesses at least one specific and substantial utility, and one of ordinary skill in the art would know how to use such a polynucleotide. Further, it is believed that undue experimentation would not be required of a skilled artisan to make and use the polynucleotides of claim 1.

Because amended claim 1 no longer recites "a polynucleotide hybridizing under stringent conditions with ... SEQ ID NO:2," the rejection of claims 1-2 and 5-7 under 35 U.S.C. § 112, first paragraph, is overcome to the extent that it is based on this subject matter. New claim 32 embraces this subject matter and further recites a hybridizing polynucleotide whose complement "detects, by microanalysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model." Therefore, the polynucleotide of claim 32 has utility based on this limitation and on its high degree of identity to SEQ ID NO: 2, as would be expected of a polynucleotide that hybridizes under the recited conditions of high stringency.

As the specification teaches how to use the invention commensurate with the scope of claims 1-2 and 5-7 as currently amended, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Rejections under 35 U.S.C. § 102(b)

(1) Claim 1 was rejected under 35 U.S.C. 102(b) "as being anticipated by Suzuki et al. (US Patent 5,719,125, 2/17/1998). The Examiner noted that Suzuki et al. teaches "the sequence of SEQ ID NO 11, a 60 mer, the complement of which contains 34 contiguous nucleotides that are identical (positions 12-45 of SEQ ID NO 11) to SEQ ID NO 2 from positions

841 to 874," and further that claim 1 has been "interpreted broadly to encompass the SEQ ID NO 11 taught by Suzuki."

(2) Claim 1 was further rejected under 35 U.S.C. 102(b) "as being anticipated by Accession number AA891470 (June 16, 1998)." The Examiner noted that AA891470 "corresponds to a nucleic acid sequence of 459 nucleotides, the complement of which, from position 1 to position 446 is almost identical (only contains 3 mismatches) to nucleotides 395 to 840 of SEQ ID NO 2," and further that claim 1 has been "interpreted broadly to encompass the sequence of AA891470.

Claim 1 as currently amended specifically recites "polynucleotides that encode a polypeptide having at least 90% sequence identity with SEQ ID NO: 1" or to specific regions thereof and further recites that the complement of such a polynucleotide "detects, by microanalysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model." Applicants point out that Suzuki et al. and AA891470 do not disclose the claimed polynucleotides as described above, but only describe *portions*, i.e. amino acids 219 to 230 of SEQ ID NO: 1 and amino acids 71 to 218 of SEQ ID NO: 1, respectively, of the claimed polynucleotides. Further, Suzuki et al. and AA891470 do not teach the additional limitation of the ability of complement of such polynucleotides to *detect by microarray analysis a polynucleotide that is differentially expressed.* Accordingly, the claims as currently amended, are not anticipated by these references.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Obviousness-type Double Patenting

Claims 1-7 were rejected under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 1 and 3-6 of copending Application No. 09/809545."

Applicants believe that upon entry of the present Amendment and consideration of the arguments presented, this will be the only rejection remaining in the present application. Accordingly, the Examiner is requested to withdraw the provisional obviousness-type double patenting rejection in the present case, allow the present application, and repeat the double patenting rejection, if appropriate, in parallel application 09/809,545.

Applicants believe that the present application is now in *prima facie* condition of allowance and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding he is respectfully requested to telephone the undersigned attorney at the telephone number indicated below.

Although no fees are believed to be due at this time, please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 17, 2002

By: _____

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